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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/643,298	08/18/2003	Ann de Wees Allen	ALL-T101D1	4203

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EXAMINER	
ROYDS, LESLIE A	
ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/643,298	ALLEN, ANN DE WEES	
	Examiner	Art Unit	
	Leslie A. Royds	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6-9 and 12-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6-9 and 12-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-3, 6-9 and 12-15 are presented for examination.

Applicant's Amendment filed November 12, 2008 has been received and entered into the present application.

Claims 1-3, 6-9 and 12-15 remain pending and under examination.

Applicant's arguments, filed November 12, 2008, have been fully considered. Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections are either reiterated or newly applied. They constitute the complete set of rejections presently being applied to the instant application.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1 and 6 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Rudman et al. ("Growth Hormone Treatment of Frailty in Men Over 60", *New England Journal of Medicine*, 1990) in view of Fulks et al. ("Effects of Insulin, Glucose, and Amino Acids on Protein Turnover in Rat Diaphragm", *J. Biol. Chem.*, 250(1); 1975:290-298) and further in view of Dudrick et al. (U.S. Patent No. 5,026,721; 1991), each already of record, for the reasons of record set forth at p.3-5 of the previous Office Action dated May 12, 2008, of which said reasons are herein incorporated by reference.

Response to Applicant's Arguments

Applicant traverses the instant rejection, stating that, at the time of the invention, arginine and lysine were typically combined because lysine inhibited the growth of herpes 1 and 2 virus, which

arginine "tends to promote" (p.2, Remarks) and alleges that a skilled artisan at the time of the current invention would have had no motivation to create a composition with arginine that did not also include lysine. Applicant alleges that Fulks et al. teaches that the effect of the branched chain amino acids is not improved by the presence of other amino acids. Still further, Applicant opines that the disclosure cannot be used to reconstruct the prior art for a rejection under 35 U.S.C. 103(a). Applicant argues against Dudrick et al., stating that the reference teaches away from the current invention because the composition of Dudrick et al. must have at least 5 amino acids or more.

Applicant's traversal has been fully and carefully considered, but fails to be persuasive.

Firstly, Applicant's arguments that the art would teach away from the exclusion of lysine from an arginine-containing composition in light of the herpes virus promoting effects of arginine are unpersuasive. Applicant's assertion that one of ordinary skill would have necessarily included lysine in combination with the arginine component is unsubstantiated by any evidence and is, therefore, not persuasive. Please reference MPEP §716.01(c)[R-2](II), which states, "The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965)." This lack of substantiating evidence aside, it is further noted that although the presence of arginine alone may not be preferable to the skilled artisan only for the reason that, as Applicant has alleged on the record, it "tends to promote" herpes virus 1 and 2, such does not constitute a teaching away from a non-preferred embodiment, which, in the present case, would be the use of arginine alone in the absence of lysine. Applicant is reminded that, in accordance with the MPEP at §2123, "A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill in the art, including non-preferred embodiments…Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or non-preferred embodiments."

Applicant's further allegation that one of skill in the art would have had no motivation to use arginine in the absence of lysine is clearly not persuasive because Applicant has provided no evidence

that the state of the art at the time of the invention was such that the skilled artisan would have only contemplated administration of arginine in combination with lysine. The fact that arginine "tended to promote" herpes virus is (1) not a guarantee that herpes virus would always develop with arginine administration, (2) not a guarantee that the absence of lysine in combination with arginine would necessarily always result in development of herpes virus and/or (3) not a teaching that the beneficial effects of arginine could only be achieved with concomitant administration of lysine to preclude the development of herpes virus. Accordingly, the conspicuous absence of any evidence in the record to support the allegation that the state of the art was such at the time of the invention that the skilled artisan would have only contemplated the administration of arginine with lysine further supports the conclusion that the skilled artisan would have viewed the administration of arginine in combination with lysine as a preferable, but not required, combination of agents.

Secondly, Applicant's allegation that Fulks et al. teaches that the effect of the branched chain amino acids is not improved by the presence of other amino acids is also unpersuasive. Applicant has taken the teachings of Fulks et al. out of context as they were set forth in the Office Action dated May 12, 2008. Please see p.3-4 of said Office Action, which states:

"Fulks et al. discloses a study of branched chain amino acids (i.e., leucine, isoleucine and valine) in regulating protein turnover in rat diaphragm muscle, wherein it was demonstrated that addition of the branched chain amino acids alone decreased protein catabolism as compared to the remaining amino acids (i.e., all but the branched chain amino acids), which did not alter the rate of protein breakdown significantly (col.1, para.3, p.295). Fulks et al. further teaches that the branched chain amino acids were also capable of stimulating protein synthesis at least to the same extent as a complete mixture of amino acids and further discloses that the branched chain amino acids also function to increase protein synthesis (col.2, para.2, p.295). Still further, Fulks et al. discloses that leucine, isoleucine and valine play a crucial role in regulating net protein balance in muscle and additionally teaches that the effects of leucine, isoleucine and valine on protein synthesis appeared to be approximately additive. Fulks et al. further notes that the factors that promoted synthesis and inhibited degradation in the incubated diaphragm have long been recognized as important for muscle growth *in vivo* (col.1, para.2, p.297)."

Note that Fulks et al. compared protein catabolic effects of the branched chain amino acids *independently* from the remaining (i.e., all but the branched chain amino acids). In other words, Applicant's allegation that "the effect of the branched chain amino acids is not improved by the presence of other amino acids" is erroneous because the protein catabolic effect of the branched chain amino acids was not studied in combination with all other remaining amino acids and, therefore, Applicant has no basis in the teachings of Fulks et al. to assume that that "the effect of the branched chain amino acids is not improved by the presence of other amino acids".

Furthermore, though Fulks et al. does not specifically study arginine in combination with the branched chain amino acids leucine, isoleucine and valine, Fulks et al. very explicitly teaches that the *branched chain amino acids (i.e., leucine, isoleucine and valine), in the absence of the remaining amino acids (i.e., all but the branched chain amino acids)*, (1) decreased protein catabolism (col.1, para.3, p.295); (2) stimulated and increased protein synthesis (col.2, para.2, p.295); and (3) had approximately additive effects on protein synthesis (col.1, para.2, p.297). These facts regarding the effects of leucine, isoleucine and valine on stimulating and increasing protein synthesis while decreasing protein catabolism (as evidenced by Fulks et al.), combined with the teaching of Rudman et al. in that arginine enhances the release of growth hormone and, thus, increased the muscle to fat ratio of the body (i.e., builds muscle mass), is clear evidence that the combination of arginine, leucine, isoleucine and valine would have been *prima facie* obvious to one of ordinary skill in the art motivated by the desire to formulate a combination of amino acids capable of increasing muscle mass. See *In re Kerkhoven*, 626 F.2d 846, 205 USPQ 1069, at page 1072 (CCPA 1980).

Thirdly, Applicant's argument that the disclosure cannot be used to reconstruct the prior art for a rejection under 35 U.S.C. 103(a) is also unimpressive. This argument is understood to be essentially tantamount to an allegation that the Examiner has used improper hindsight to formulate the *prima facie* case of obviousness. This is unpersuasive. Any judgment on obviousness is, *in a sense*, necessarily a

reconstruction based upon hindsight reasoning. However, so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the Appellant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). Considering the fact that the present rejection under 35 U.S.C. 103(a) relies solely on the knowledge and motivation that was generally available to one of ordinary skill in the art at the time of the invention (as clearly elucidated *supra*, as well as in each of the previous Office Actions) and does *not* (contrary to Applicant's allegations) improperly rely upon Applicant's disclosure, the assertion that the present rejection is made with impermissible hindsight reconstruction is unpersuasive.

Fourthly, and lastly, Applicant's argument against Dudrick et al., stating that the reference teaches away from the current invention because the composition of Dudrick et al. must have at least 5 amino acids or more, is also unpersuasive. The reliance upon Dudrick et al. was not made to bodily incorporate the features of the reference into Rudman et al. in view of Fulks et al. Rather, it was relied upon for its teaching that, specifically, the L-form of amino acids were known in the art to be more biologically active than the D-form of the same. The fact that Dudrick et al. may disclose the use and/or incorporation of additional amino acids aside from the four specifically and instantly claimed does not negate the teaching that the L-form of amino acids is more biologically active than the D-form. Accordingly, in view of such a teaching of Dudrick et al., it remains that the use of the more biologically active L-form would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention seeking to create the most efficacious and biologically active composition possible, absent factual evidence to the contrary. Moreover, Applicant is again reminded that the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference, nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the *combined teachings* of the references would have suggested to

those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). In the instant case, the basis of the rejection is not grounded in the idea of bodily incorporating all of the features of Dudrick et al. into the other cited prior art references, but rather to *combine* the knowledge (i.e., in this case, that the L-form of amino acids is more biologically active than the D-form) of Dudrick et al. with that of the other cited prior art. Thus, Applicant's allegation that Dudrick et al. teaches away from the instantly claimed invention is unpersuasive for these reasons.

For these reasons *supra*, and those previously made of record at p.3-5 of the Office Action dated May 12, 2008, rejection of claims 1 and 6 remains proper.

Claims 1-3 and 6-9 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Rudman et al. ("Growth Hormone Treatment of Frailty in Men Over 60", *New England Journal of Medicine*, 1990) in view of Fulks et al. ("Effects of Insulin, Glucose, and Amino Acids on Protein Turnover in Rat Diaphragm", *J. Biol. Chem.*, 250(1); 1975:290-298) and Dudrick et al. (U.S. Patent No. 5,026,721; 1991) and further in view of Boynton et al. (U.S. Patent No. 5,087.624; Issued 1992, Priority to 1987) and Remington's Pharmaceutical Sciences (Sixteenth Edition, 1980, p.669-671), each already of record, for the reasons set forth at p. 5-8 of the previous Office Action dated May 12, 2008, of which said reasons are herein incorporated by reference.

Response to Applicant's Arguments

Applicant traverses the instant rejection, stating that the shortcomings of the primary references have already been discussed *supra*. Applicant alleges that "Rudman et al. teach the skilled artisan very little at all, and certainly the Rudman et al. reference does not provide any expectation that the Applicant's specific four-amino acid composition would be advantageous" (p.4, Remarks). Applicant opines that, if Fulks et al. "teaches anything relevant it would be that the branched chain amino acids should be used alone" (p.4, Remarks). Still further, Applicant alleges that Dudrick et al. teaches away from the current

invention and neither Boynton et al. nor Remington's addresses "these issues at all" (p.5, Remarks). Applicant alleges it is "difficult to ascertain how, in the absence of the current applicant's disclosure...even if these references were chosen, how they would motivate one skilled in the art to arrive at the applicant's specific composition" (p.5, Remarks).

Applicant's traversal has been fully and carefully considered, but fails to be persuasive.

Firstly, regarding Applicant's allegations against the primary references, the remarks provided *supra* with regard to the primary references are incorporated by reference herein in response. Applicant is referenced above to such a discussion, which will not be repeated herein in the interests of brevity in the record.

Secondly, the allegation that "Rudman et al. teach the skilled artisan very little at all" is not a point well taken. Rudman et al. very clearly provides extensive and relevant teachings of the prior art, which are summarized at p.3 of the Office Action dated May 12, 2008. To assert that Rudman et al. provides no relevant teachings to the skilled artisan is erroneous and contradictory to the facts. This argument, therefore, is unimpressive.

Thirdly, Applicant's allegation that Rudman et al. fails to provide any expectation that the Applicant's specific four-amino acid composition would be advantageous is strongly disputed. Rudman et al. very clearly teaches that arginine enhances the release of growth hormone and, thus, increased the muscle to fat ratio of the body (i.e., builds muscle mass). These facts regarding arginine, combined with the teachings of Fulks et al., who Fulks et al. very explicitly teaches that the branched chain amino acids (i.e., leucine, isoleucine and valine) (1) decreased protein catabolism (col.1, para.3, p.295); (2) stimulated and increased protein synthesis (col.2, para.2, p.295); and (3) had approximately additive effects on protein synthesis (col.1, para.2, p.297), is clear evidence that the combination of arginine, leucine, isoleucine and valine would have been *reasonably expected*, when combined, to provide a composition effective for the purpose of stimulating muscle growth in view of the fact that each amino acid was

known to function to increase muscle mass. As a result, such a reasonable expectation of success clearly supports the *prima facie* obviousness of such a combination to formulate a combination of amino acids capable of increasing muscle mass based upon the shared therapeutic utility of each of the four specified amino acids. See *In re Kerkhoven*, 626 F.2d 846, 205 USPQ 1069, at page 1072 (CCPA 1980).

Fourthly, Applicant's conclusion that the only allegedly "relevant" teaching of Fulks et al. is that "the branched chain amino acids should be used alone" (p.4, Remarks) is unimpressive. Fulks et al. provides no such explicit teaching that the branched chain amino acids must be used alone and never combined with any other amino acids to render the effect of generating increased protein synthesis. This is Applicant's subjective characterization of what he views to be "the only relevant teaching" of the reference and clearly ignores the full scope of prior art teachings, both explicit and implicit, obtained from the disclosure of Fulks et al. Furthermore, Applicant fails to point to any portion of the reference that allegedly provides support for what he views to be this "only relevant teaching" of the reference. As a result, this point is unpersuasive, particularly in view of the fact that, for the reasons described *supra*, one of ordinary skill in the art *would have been* motivated to combine the branched chain amino acids with arginine based upon their shared therapeutic utility in increasing muscle mass.

Fifthly, Applicant argues against Dudrick et al., stating that the reference teaches away from the current invention, but fails to advance any reasons to support his position to this effect. Accordingly, such a remark is not found persuasive. Moreover, the remarks that "Boynton et al. do not address these issues at all, nor does the Remington's reference" are also found unpersuasive because it is unclear what issues are, in fact, circumscribed by the phrase "these issues" such that it would be clear to the Examiner exactly what argument is being made. Since Applicant does not describe what is meant by the phrase "these issues" in detail, the remarks are unpersuasive.

Sixthly, and lastly, Applicant alleges it is "difficult to ascertain how, in the absence of the current applicant's disclosure...even if these references were chosen, how they would motivate one skilled in the

art to arrive at the applicant's specific composition" (p.5, Remarks) This is also unpersuasive. The Examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). However, in the instant case, extensive reasoning regarding the motivation to combine the cited references to arrive at Applicant's instantly claimed composition was provided at p.3-8 of the previous Office Action dated May 12, 2008, upon which the Examiner again relies to support the *prima facie* case of obviousness, which will not be repeated herein so as not to burden the record. Applicant's attention is again directed thereto.

For these reasons *supra*, and those previously made of record at p.5-8 of the Office Action dated May 12, 2008, rejection of claims 1-3 and 6-9 remains proper.

Claims 12 and 14 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Cerra et al. (U.S. Patent No. 4,780,475; 1988) in view of Rudman et al. ("Growth Hormone Treatment of Frailty in Men Over 60", *New England Journal of Medicine*, 1990) and further in view of Fulks et al. ("Effects of Insulin, Glucose, and Amino Acids on Protein Turnover in Rat Diaphragm", *J. Biol. Chem.*, 250(1); 1975:290-298) and Dudrick et al. (U.S. Patent No. 5,026,721; 1991), each already of record, for the reasons of record set forth at p.8-11 of the previous Office Action dated May 12, 2008, of which said reasons are herein incorporated by reference.

Response to Applicant's Arguments

Applicant traverses the instant rejection, stating that Cerra et al. discloses a composition with an extensive array of amino acids and, thus, it is "extremely hard to understand" (p.5, Remarks) how such a reference can render obvious Applicant's composition with only four specific amino acids. Applicant

argues that the secondary references fail to provide any teachings to motivate the skilled artisan to remove most of the amino acids from the Cerra et al. composition. Applicant alleges that "Rudman et al. teach the skilled artisan very little at all, and certainly the Rudman et al. reference does not provide any expectation that the Applicant's specific four-amino acid composition would be advantageous" (p.5, Remarks). Applicant opines that, if Fulks et al. "teaches anything relevant it would be that the branched chain amino acids should be used alone" (p.5, Remarks). Still further, Applicant alleges that Dudrick et al. teaches away from the current invention and alleges the one of skill in the art at the time of the invention would not have found it obvious to create a composition with arginine that did not include lysine because lysine with arginine was used to prevent herpes virus infections.

Applicant's traversal has been fully and carefully considered, but fails to be persuasive.

Firstly, Applicant's allegation that Cerra et al. Discloses a composition with an extensive array of amino acids and, thus, it is "extremely hard to understand" (p.5, Remarks) how such a reference can render obvious Applicant's composition with only four specific amino acids is unpersuasive. The Office Action explicitly noted this as a difference between the reference to Cerra et al. taken alone and the instant claims. However, such a difference was remedied by the citation to Fulks et al. because, though Cerra et al. discloses the use of additional amino acids in the composition disclosed by this reference, one of ordinary skill in the art at the time of the invention would have found it *prima facie* obvious to administer L-leucine, L-isoleucine and L-valine with arginine but in the absence of other essential or non-essential amino acids because Fulks et al. teaches that branched chain amino acids alone decreased protein catabolism as compared to the remaining amino acids (i.e., all but the branched chain amino acids), which did not alter the rate of protein breakdown significantly (col. 1, para.3, p.295). Fulks et al. further teaches that the branched chain amino acids were also capable of stimulating protein synthesis at least to the same extent as a complete mixture of amino acids and further discloses that the branched chain amino acids also function to increase protein synthesis (col.2, para.2, p.295). In view of such a

teaching, such a person skilled in the art would have been motivated to administer the combination of L-leucine, L-isoleucine and L-valine with arginine in the absence of the other essential and non-essential amino acids disclosed in Cerra et al. because, as evidenced by Fulks et al., the branched chain amino acids were more effective in decreasing protein catabolism than all other amino acids combined but the branched chain amino acids. This is, contrary to Applicant's allegations, a clear motivation to administer the four claimed amino acids in the absence of the other essential and non-essential amino acids disclosed in Cerra et al.

Furthermore, Applicant's allegation that Cerra et al. alone does not teach the four specifically claimed amino acids does not appreciate the fact that a citation to Fulks et al. was made to remedy this shortcoming of the primary reference to Cerra et al. Applicant is reminded that rejections made under 35 U.S.C. 103(a) are based upon the combination of references. As a result, focusing solely on the discrete teachings of each of the cited references (i.e., in this case, considering Cerra et al. alone without considering it as it was combined with the cited secondary reference(s)) is tantamount to examining each of them inside of a vacuum and fails to be persuasive in establishing non-obviousness because it is the *combined* teachings that are the basis for a proper conclusion of obviousness, not each individual reference alone. In other words, it must be remembered that the references are relied upon in combination and are not meant to be considered separately. To properly conclude obviousness of an invention *does not require the claimed invention to be expressly suggested in its entirety by any one single reference under 35 U.S.C. 103(a).* Rather, the test is *what the combined teachings* of the references would have suggested to those of ordinary skill in the art. Please reference *In re Young*, 403 F.2d 754, 159 USPQ 725 (CCPA 1968) and *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981).

Secondly, the allegation that "Rudman et al. teach the skilled artisan very little at all" is not a point well taken. Rudman et al. very clearly provides extensive and relevant teachings of the prior art, which are summarized at p.3 of the Office Action dated May 12, 2008. To assert that Rudman et al.

provides no relevant teachings to the skilled artisan is erroneous and contradictory to the facts. This argument, therefore, is unimpressive.

Thirdly, Applicant's allegation that Rudman et al. fails to provide any expectation that the Applicant's specific four-amino acid composition would be advantageous is strongly disputed. Rudman et al. very clearly teaches that arginine enhances the release of growth hormone and, thus, increases the muscle to fat ratio of the body (i.e., builds muscle mass). These facts regarding arginine, combined with the teachings of Cerra et al. in view of Fulks et al., wherein Cerra et al. teaches an amino acid composition functional to decrease protein catabolism and improve protein synthesis in stressed patients, such as septic patients, and Fulks et al. teaches that the branched chain amino acids (i.e., leucine, isoleucine and valine) (1) decreased protein catabolism (col.1, para.3, p.295); (2) stimulated and increased protein synthesis (col.2, para.2, p.295); and (3) had approximately additive effects on protein synthesis (col.1, para.2, p.297), is clear evidence that the combination of arginine, leucine, isoleucine and valine would have been *reasonably expected*, when combined, to provide a composition effective for the purpose of stimulating muscle growth and decreasing protein catabolism, particularly in stressed patients, such as septic patients, who experience an extremely high and rapid rate of muscle protein catabolism (as evidenced by Cerra et al.) in view of the fact that each amino acid was known to function to increase muscle mass. As a result, such a reasonable expectation of success clearly supports the *prima facie* obviousness of such a combination to formulate a combination of amino acids capable of increasing muscle mass based upon the shared therapeutic utility of each of the four specified amino acids. See *In re Kerkhoven*, 626 F.2d 846, 205 USPQ 1069, at page 1072 (CCPA 1980).

Fourthly, Applicant's conclusion that the only allegedly "relevant" teaching of Fulks et al. is that "the branched chain amino acids should be used alone" (p.4, Remarks) is unimpressive. Fulks et al. provides no such explicit teaching that the branched chain amino acids must be used alone and never combined with any other amino acids to render the effect of generating increased protein synthesis. This

is Applicant's subjective characterization of what he views to be "the only relevant teaching" of the reference and clearly ignores the full scope of prior art teachings, both explicit and implicit, obtained from the disclosure of Fulks et al. Furthermore, Applicant fails to point to any portion of the reference that allegedly provides support for what he views to be this "only relevant teaching" of the reference. As a result, this point is unpersuasive, particularly in view of the fact that, for the reasons described *supra*, one of ordinary skill in the art *would have been* motivated to combine the branched chain amino acids with arginine based upon their shared therapeutic utility in increasing muscle mass.

Fourthly, Applicant's argument against Dudrick et al., stating that the reference teaches away from the current invention because the composition of Dudrick et al. contains lysine, is also unpersuasive. The reliance upon Dudrick et al. was not made to bodily incorporate the features of the reference into the cited references to Cerra et al., Rudman et al. and Fulks et al. Rather, it was relied upon for its teaching that, specifically, the L-form of amino acids were known in the art to be more biologically active than the D-form of the same. The fact that Dudrick et al. may disclose the use and/or incorporation of additional amino acids, such as, e.g., lysine, aside from the four specifically and instantly claimed does not negate the teaching that the L-form of amino acids is more biologically active than the D-form. Accordingly, in view of such a teaching of Dudrick et al., it remains that the use of the more biologically active L-form would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention seeking to create the most efficacious and biologically active composition possible, absent factual evidence to the contrary. Moreover, Applicant is again reminded that the test for obviousness is not whether the features of a secondary reference may be bodily incorporated into the structure of the primary reference, nor is it that the claimed invention must be expressly suggested in any one or all of the references. Rather, the test is what the *combined teachings* of the references would have suggested to those of ordinary skill in the art. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981). In the instant case, the basis of the rejection is not grounded in the idea of bodily incorporated all of the features

of Dudrick et al. into the other cited prior art references, but rather to *combine* the knowledge (i.e., in this case, that the L-form of amino acids is more biologically active than the D-form) of Dudrick et al. with that of the other cited prior art. Thus, Applicant's allegation that Dudrick et al. teaches away from the instantly claimed invention is unpersuasive for these reasons.

Fifthly, and lastly, Applicant again appears to be arguing that one of skill in the art would only have administered lysine with arginine because the art would teach away from excluding lysine from an arginine-containing composition because of the herpes virus promoting effects of arginine are unpersuasive. Applicant's assertion that one of ordinary skill would have necessarily included lysine in combination with the arginine component is unsubstantiated by any evidence and is, therefore, not persuasive. Please reference MPEP §716.01(c)[R-2](II), which states, "The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965)." This lack of substantiating evidence aside, it is further noted that although the presence of arginine alone may not be preferable to the skilled artisan only for the reason that, as Applicant has alleged on the record, it "tends to promote" herpes virus 1 and 2, such does not constitute a teaching away from a non-preferred embodiment, which, in the present case, would be the use of arginine alone in the absence of lysine. Applicant is reminded that, in accordance with the MPEP at §2123, "A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill in the art, including non-preferred embodiments…Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or non-preferred embodiments."

Applicant has provided no evidence that the state of the art at the time of the invention was such that the skilled artisan would have only contemplated administration of arginine in combination with lysine. The fact that arginine tended to promote herpes virus is (1) not a guarantee that herpes virus would always develop with arginine administration, (2) not a guarantee that the absence of lysine in combination with arginine would necessarily always result in development of herpes virus and/or (3) not

a teaching that the beneficial effects of arginine could only be achieved with concomitant administration of lysine to preclude the development of herpes virus. Accordingly, the conspicuous absence of any evidence in the record to support the allegation that the state of the art was such at the time of the invention that the skilled artisan would have only contemplated the administration of arginine with lysine further supports the conclusion that the skilled artisan would have viewed the administration of arginine in combination with lysine as a preferable, but not required, combination of agents.

For these reasons *supra*, and those previously made of record at p.8-11 of the Office Action dated May 12, 2008, rejection of claims 12 and 14 remains proper.

Claims 12-15 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Cerra et al. (U.S. Patent No. 4,780,475; 1988) in view of Rudman et al. ("Growth Hormone Treatment of Frailty in Men Over 60", *New England Journal of Medicine*, 1990) and further in view of Fulks et al. ("Effects of Insulin, Glucose, and Amino Acids on Protein Turnover in Rat Diaphragm", *J. Biol. Chem.*, 250(1); 1975:290-298) and Dudrick et al. (U.S. Patent No. 5,026,721; 1991) and Remington's Pharmaceutical Sciences (Sixteenth Edition, 1980; p.669-671), each already of record, for the reasons of record set forth at p.11-12 of the previous Office Action dated May 12, 2008, of which said reasons are herein incorporated by reference.

Response to Applicant's Arguments

Applicant traverses the instant rejection, stating that the cited references, either taken alone or in combination, do not disclose or suggest the Applicant's advantageous composition, or its use for stimulating muscle growth.

Applicant's traversal has been fully and carefully considered, but fails to be persuasive.

Applicant's statement that the references taken alone or in combination do not disclose or suggest the Applicant's advantageous composition or its use for stimulating muscle growth is unpersuasive in

view of the fact that Applicant advances no reasons to support his position. Accordingly, the Examiner defers to the explanation provided in the body of the previous Office Action at p.11-12 as to why the references, in combination, teach the instantly claimed invention. Such reasons will not be repeated herein so as not to burden the record.

For these reasons *supra*, and those previously made of record at p.11-12 of the Office Action dated May 12, 2008, rejection of claims 12-15 remains proper.

Conclusion

Rejection of claims 1-3, 6-9 and 12-15 remains proper.

No claims of the present application are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie A. Royds whose telephone number is (571)-272-6096. The examiner can normally be reached on Monday-Friday (9:00 AM-5:30 PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571)-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leslie A. Royds/
Patent Examiner, Art Unit 1614

February 10, 2009

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614